EXHIBIT A

BIOGRAPHICAL SKETCH

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NAME: **Rhonda R. Voskuhl, M.D.**

eRA COMMONS USER NAME (credential, e.g., agency login): VOSKUHL2

POSITION TITLE: **Professor of Neurology, Jack H. Skirball Chair**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Phillips University, Enid, OK	BS	05/1982	Biology
Vanderbilt Medical School, Nashville, TN	MD	06/1986	Medicine
Univ. of Texas Southwestern, Dallas, TX	Resident	06/1990	Neurology
NIH, Neuroimmunology Branch, Bethesda, MD	Fellow	04/1995	Neuroimmunology

A. Personal Statement

I have devoted my career to translational research based on clinical observations in patients using a "Bedside to Bench to Bedside" approach: Initially focusing on key clinical observations, disentangling underlying mechanisms at the lab bench, then designing clinical trials of new treatments based on these mechanisms. A key foundational clinical observation is the effect of being female versus male on MS and other neurodegenerative conditions, including aging. I am an internationally recognized expert in sex differences research, demonstrating protective effects of estrogen and testosterone treatment in preclinical models, which I translated to four clinical trials in patients. My lab was the first to show that estrogen receptor (ER) alpha and ER beta ligands act through distinct mechanisms to induce neuroprotection. I showed that ER beta ligation induced remyelination through direct action on oligodendrocytes, while downregulating innate immunity via actions on microglia. I also discovered that an X chromosome gene (the histone demyethylase *Kdm6a*) increases neuroinflammation. In addition, my lab was the first to use brain cell-specific and region-specific transcriptomics to investigate the molecular basis for disability-specific disease progression in MS. We use MS postmortem tissues from human subjects as well as human gene databases to validate genes identified in preclinical models. We have shown disability-specific brain atrophy in MS patients. My lab also investigates the role of brain aging on neurodegeneration, identifying a sex hormone by age interaction whereby being estrogen deficient and midlife combine to induce cognitive decline, dorsal hippocampal atrophy, glial activation, and synaptic loss. This is mediated by loss of ER beta in astrocytes and suggests a target to prevent disability worsening in women during menopause. The goal of my research is to use a brain region-specific, cell-specific, and sex-specific approach to identify neuroprotective treatment targets, then design clinical trials to repair neurodegeneration which are optimally tailored for sex and age. In the clinic I see patients with MS, and I am the faculty neurologist for the UCLA Comprehensive Menopause Program where I see otherwise healthy women with cognitive deficits during menopause.

Active funding: (suspended as of July 31, 2025)

R35 Research Program Awardee for 2023 (To approximately 10-15 neuroscientists per year across the U.S.)
NIH NINDS 05/15/2023 – 04/30/2031 Total $7,270,927
#R35NS132150 (PI Voskuhl)
Title: Neurodegeneration Underlying Distinct Disabilities in Multiple Sclerosis Using a Cell-Specific, Region-Specific, and Sex-Specific Approach
Goal: Develop treatments tailored for women and men that target neurodegenerative processes within the brain to repair disabilities.

Recent Publications to Highlight:

Deletion of the X gene, *Kdm6a*, in microglia reverses the disease-associated microglia transcriptome. ***Science Translational Medicine****,* in press, 2025.

Estrogen receptor beta in astrocytes modulates cognitive function in mid-age female mice**.** ***Nature Communications*** https://doi.org/10.1038/s41467-023-41723-7, Sept 29, 2023.

Together these two papers show the clinically relevant balance between: 1) a female sex chromosome (XX) gene which drives neuroinflammation and neurodegeneration in MS as well as brain aging in healthy females (as compared to men who are XY), *versus* 2) a female sex hormone (estrogen) which is anti-inflammatory and neuroprotective (as compared to men who have testosterone). This estrogen mediated neuroprotection is lost abruptly at menopause in women age 50-53 years, while testosterone mediated neuroprotection is lost gradually during andropause in men from age 30 to 70 years.

Reviews & Commentaries:
Voskuhl, R. Itoh, Y. The X factor in neurodegeneration. **Journal of Experimental Medicine,** Nov. 5, 2022.
Voskuhl, R., A new cell subtype that confers neuroprotection. **Nature Immunology**, Nov. 3, 2020.
Voskuhl, R., Klein, S., Sex is a biological variable - in the brain too. **Nature**, 568 (7751):171, 2019.
Voskuhl, R., Wang, H., Elashoff, R. Why use sex hormones in relapsing-remitting multiple? **Lancet Neurology**, 15:790, 2016.
Voskuhl, R., Gold, S. Sex-related factors in multiple sclerosis susceptibility and progression. **Nature Reviews Neurology,** 8:255, 2012.

B. Positions and Honors

Positions and Employment

2004-present Professor, Dept. of Neurology, UCLA, Los Angeles, CA
2023-present Faculty Neurologist, UCLA Comprehensive Menopause Program, Los Angeles, CA
2000-present Director, UCLA Multiple Sclerosis Program, UCLA, Los Angeles, CA
2000-2004 Associate Professor, Dept. of Neurology, UCLA, Los Angeles, CA
1995-2000 Scientific Director, UCLA Multiple Sclerosis Program, UCLA, Los Angeles, CA
1995-2000 Assistant Professor, Dept. of Neurology, UCLA, Los Angeles, CA
1994-1995 Senior Investigator, Neuroimmunology Branch, NIH, Bethesda, MD
1993-1994 Research Associate, Lab of Viral and Molecular Pathogenesis, NIH, Bethesda, MD
1990-1993 Clinical Associate, Neuroimmunology Branch, NIH, Bethesda, MD

Honors

2024-John Dystel Prize in Multiple Sclerosis, the most prestigious award in the field of MS.
2024-Lancet Neurology: Career Profile (February issue).
2023-Rachel Horne Prize in Women's Health Research in MS, ECTRIMS/ACTRIMS meeting Milan, 2023
2019-Kenneth P. Johnson Memorial Lecture, ACTRIMS annual meeting 2019
2018-Berlin Institute of Health (BIH) Excellence Award for Sex and Gender Aspects in Health Research
2018-UCLA Innovation Award, UCLA Campus-wide Technology Development Group Competition for 2018
2006-Jack H. Skirball Chair in MS Research
2001-California Congressman Henry Waxman Honorary Grant
1997-Harry Weaver Neuroscience Scholar of the National Multiple Sclerosis Society (NMSS)
1995-Outstanding Young Alumna, Phillips University
1994-Public Health Service Citation for Excellence in Research, National Institutes of Health (NIH)
1991-Annual Noble Lectureship Award
1988 and 1990-Texas Neurologic Society Annual Research Award for a Neurology Resident (twice)
1982-Oklahoma College All Star Women's Basketball Team
1982-Representative Phillipian - Overall Most Outstanding Senior Award, Phillips University
1979-1982-Biology Award (1979), Chemistry Award (1980), Science Award (1982), Phillips University
1978-1982-Four year full basketball scholarship - Two year Team Captain, Phillips University

Other Experience and Professional Memberships

Department of Defense (DOD) Congressionally Directed Medical Research Program's (CDMRP) Multiple Sclerosis Research Program (MSRP), Programmatic Panel, member, 2020-2023.

Member, NIH Study Section BDCN, 2002-2006; NIH Special Emphasis Panel NSD-C, 2009-2012; NIH Study Section Ad hoc: NSD-C / NSD-A, 2013-2017; HAI, 2018-2019; CNBT, 2021; Special Emphasis Panel review of Program Project Grants, NIAID, 2022; BRAIN Initiative Cell Atlas Network (BICAN) grants, NIH /

NIMH ZMH1 ERB-L (06), 2023, NIH ZNS1-SRB-E NINDS R35 Review Panel B, 2024. NIH Special Emphasis Panel, Aging Systems and Geriatrics study section NIH/CSR, 2025.

Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) Steering Committee, 2007-2012: ACTRIMS Advisory Committee, 2015-present; ACTRIMS Resident Summit, 2017-2023; ACTRIMS Young Scientist Summit, 2018-2023.

European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS), Faculty, 2023-present.

Presidential Leadership 6 year commitment to the Organization for the Study of Sex Differences (OSSD), President-Elect, 2018-2020; President, 2020-2022; Past-President, 2022-2024; OSSD Annual Meeting Organizing Committee, 2016-2018; NIH Office of Research on Women's Health (ORWH) / FDA Office of Women's Health Sex and Gender online course, 2019-2022.

Deutsche Forschungsgemeinschaft (DFG), German Federal Government for Excellence Cluster Initiatives, Clusters of Excellence Advisory Board Member, 2021-present.

Lead Principle Investigator for UCLA, Nancy Davis Center Without Walls, Race to Erase MS, 2019-present.

UCLA Comprehensive Menopause Care Program, Faculty Neurologist, 2023-present.

UCLA inventor on over 15 issued patents in the U.S. and Europe for a new treatment for neuroprotection: estriol treatment of cognitive decline during aging in otherwise healthy women, estriol treatment to prevent disability worsening and brain atrophy in MS women (R. Voskuhl sole inventor); novel ER beta ligand treatments for neuroprotection (R. Voskuhl & M. Jung, Co-Inventors). Co-Founder and Science Director for start-up (CleopatraRX) that licensed U.S. patents for a treatment to prevent cognitive issues of menopause.

C. Contributions to Science: Selected publications.

1. Clinical trials. I have translated basic findings from my lab on the effect of sex hormones in MS models to clinical trials in women and men with MS. First, I translated my lab's preclinical finding that the estrogen of pregnancy (estriol) is anti-inflammatory and neuroprotective. This had implications for mechanisms underlying the protection of pregnancy in MS. Translation entailed three clinical trials (2 multisite and 1 single site). The first estriol trial showed a reduction in enhancing lesions (*Annals of Neurology).* The 16 site estriol trial showed a reduction in relapses as powered as the primary outcome for a Phase 2 trial and an improvement in cognition as an exploratory (*Lancet Neurology* and featured by a Commentary). We then mapped estriol treatment induced sparing atrophy in cerebral cortex (*Brain & Behavior,* 2018), and showed an estriol treatment mediated reduction in serum neurofilament light chain (sNfL) levels (*Ann. Clin. & Trans, Neurol***.**, 2022). My lab was also the *first to show that testosterone treatment is protective in EAE* (*J. Immunology*, 159:3-6, 1997). We translated this to a pilot clinical trial in MS men (*Archives of Neurology* 64:683-688, 2007, aka *JAMA Neurology*), then mapped regions of testosterone mediated sparing of gray matter atrophy in MS men (*Neuroimage Clinical,* 4:454-460, 2014*).*

a. Sicotte, N., Liva, S.M., Klutch, R., Pfieffer, P., Bouvier, S., Odesa, S., Wu, T.C.J., Voskuhl, R.R. (2002) Treatment of multiple sclerosis with the pregnancy hormone estriol. **Annals of Neurology,** 52:421-428.

b. Voskuhl, R.R., Wang, H., and the Estriol Trial Study Group (2016) Estriol combined with glatiramer acetate for women with relapsing-remitting MS: A Randomised, Placebo-Controlled, Phase 2 Trial. **Lancet Neurology**, 15: 35-46. PMID 26621682.

*(Commentary: Voskuhl, R., Wang, H., Elashoff, R. **Lancet Neurology,** 2016, 15:790-791)

c. MacKenzie-Graham, A., Brook, J., Kurth, F., Itoh, Y., Meyer, C., Montag, M., Wang, H., Elashoff, R., Voskuhl, R.R. (2018) Estriol-mediated neuroprotection in multiple sclerosis localized by voxel-based morphometry. 8(9):e01086. **Brain & Behavior,** PMCID: PMC6160650.

d. Voskuhl, R.R., Kuhle J., Siddarth , P., Itoh, N., Patel, K., MacKenzie-Graham, A. (2022) Decreased Neurofilament Light Chain Levels In Estriol-Treated Multiple Sclerosis. **Annals of Clinical & Translational Neurology,** 9(8):1316-1320. PMID: 35770318.

e. Voskuhl, R.R. (2024) All women with multiple sclerosis should start hormone replacement therapy at menopause unless contraindicated: Yes. **Multiple Sclerosis Journal (MSJ)** 30(9):1107-1109. PMC11363466.

2. Identified the cell that mediates estrogen's neuroprotective effect *in vivo*. Estrogens were known to be neuroprotective through actions on estrogen receptors (ERs) for decades, however which cell in the CNS mediated this neuroprotection *in vivo* remained unknown. My lab created cell-specific knock outs of ER alpha and ER beta to determine which CNS cell mediated neuroprotection *in vivo*. *My lab was the first to identify which cell is responsible for estrogen mediated neuroprotection in vivo in any neurological disease model.* Most recently, we showed that Estriol and ER beta ligand treatment can induce remyelination in cerebral cortex

in the MS preclinical model, and showed that decreased ligation of ER beta in astrocytes in dorsal hippocampus mediates cognitive decline, dorsal hippocampal atrophy, and glial activation and synaptic loss in mid-life females in a preclinical model of menopause in otherwise healthy women.
a. Tiwari-Woodruff, S., Morales, L., Lee, R., Voskuhl, R.R. (2007) Differential Neuroprotective and Anti-inflammatory Effects of Estrogen Receptor (ER) α and ER β Ligand Treatment. **Proceedings of the National Academy of Sciences (PNAS),** 104:14813-14818, PMCID: PMC1976208.
b. Spence, R., Hamby, M., Umeda, E., Itoh, N., Du, S., Bondar, G., Lam, J., Ao, Y., Wisdom, A., Cao, Y., Sandoval, F., Sofroniew, M.V., Voskuhl, R.R. (2011) Neuroprotection mediated through estrogen receptor alpha on astrocytes. **Proceedings of the National Academy of Sciences (PNAS),** 108:8867-8872. PMCID: PMC3102368.
c. Spence, R.D., Wisdom, A.J., Cao, Y., Hill, H.M., Mongerson, C., Stapornkul, B., Itoh, N., Sofroniew, M.V., Voskuhl, R.R. (2013) Estrogen signaling through ER-alpha but not ER-beta on astrocytes mediates neuroprotection during EAE and decreases astrocyte levels of proinflammatory chemokines. **Journal of Neuroscience,** 33:10924-109333. PMCID: PMC3693061.
d. Kim, R., Hoffmann, A., Mangu, D. Kavosh, R., Jung, E., Itoh, N., Voskuhl, R.R. (2018) Estrogen Receptor Beta Ligand Acts on CD11c$^+$ Cells to Mediate Protection in Experimental Autoimmune Encephalomyelitis. **Brain**, 141:132-147. PMCID: PMC5837360.
e. Meyer, C.E., Smith, A.W., Padilla-Requerey A.A., Farkhondeh, V., Itoh, N., Itoh, Y., Gao, J.L., Herbig, P.D., Nguyen, Q., Ngo, K.H., Oberoi, M.R., Siddarth, P., Voskuhl, R.R., MacKenzie-Graham, A. (2023) Neuroprotection in cerebral cortex induced by the pregnancy hormone estriol. **Laboratory Investigation**, 103: 8, 100189.
f. Itoh, N., Itoh, Y., Meyer, C.S., Suen, T., Cortez Delgado, D., Rivera Lomeli, M., Wendin, S., Somepall, S.S., Golden, L., MacKenzie-Graham, A., Voskuhl, R.R. (2023) Estrogen receptor beta in astrocytes modulates cognitive function in mid-age female mice**. Nature Communications***.* https://doi.org/10.1038/s41467-023-41723-7

3. Sex chromosome effects on autoimmunity and neurodegeneration. *My lab was the first to show sex differences in EAE using its relapsing-remitting model* (*Annals of Neurology,* 39:724-733, 1996). Over the last decade, my research has been discussed by others in *Nature* editorials three times regarding how sex differences can lead to insights into disease. I also am first author of an editorial on the subject (*Nature*, 568:171, 2019). My lab discovered sex chromosome effects in the immune system in both the MS and lupus models. We then identified a gene on the X chromosome (*Kdm6a*) that escapes X-inactivation in CD4+T lymphocytes as a mechanism for increased susceptibility of females to autoimmune disease. Also, we published that parental imprinting of the X chromosome can lead to sex differences in autoimmunity. Focusing on the CNS, we showed that in contrast to XX conferring an increase in autoimmunity, XY confers an increase in the neurodegenerative response to the same autoimmune attack. Indeed, *my lab was the first to show an effect of sex chromosome complement in the CNS in any neurodegenerative disease model* (in 2014). See below for special recognition, commentaries, and editorial highlights of publications in this field.
a. Smith-Bouvier, D.L., Divekar, A.A., Sasidhar, M., Du, S., Tiwari-Woodruff, S., King, J.K., Arnold, A.P., Voskuhl, R.R. **(**2008) A role for sex chromosome complement in the female bias in autoimmune disease. **Journal of Experimental Medicine,** 20205(5):1099-108, PMCID: PMC2373842.
b. Du, S., Itoh, I., Askarinam, S., Hill, H., Arnold, A., Voskuhl, R.R. (2014) XY Sex Chromosome Complement, Compared with XX, in the CNS Confers Greater Neurodegeneration During EAE. **Proceedings of the National Academy of Sciences (PNAS),** 111:2806-2811. PMCID: PMC3932937.
*(Recognized in ***Lancet Neurology*** as one of the top 5 in MS for 2014).
c. Itoh, Y., Golden, L., Itoh, N., Matsukawa, M., Ren, E., Tse, V., Arnold, A.P., Voskuhl, R.R. (2019) The X-linked histone demethylase *Kdm6a* in CD4+ T lymphocytes modulates autoimmunity. **Journal of Clinical Investigation (JCI),** https://doi.org/10.1172/JCI126250, 130:3852-3863, PMCID: PMC6715385.
*(Commentary on this article in **JCI** 130:3536-3538, 2019.)
d. Golden, L.C., Itoh, Y., Itoh, N, Iyengar, S., Coit, P., Salama, Y., Arnold, A.P., Sawalha AH, Voskuhl, R.R. (2019) Parent-of-origin differences in DNA methylation of X chromosome genes in T lymphocytes. **Proceedings of the National Academy of Sciences (PNAS),** PMCID: PMC6936674.
*(Editorial Highlight of this paper “In This Issue” section **PNAS**.)
e. Voskuhl, R.R., Itoh, Y. (2022) The X Factor in Neurodegeneration. **Journal of Experimental Medicine**, 10.1084/jem.20211488.
f. Itoh, Y., Itoh, N., Wendin, S., Higgins, N., Voskuhl, R.R., (2025) Deletion of the X gene, *Kdm6a*, in microglia

reverses the disease-associated microglia transcriptome. **Science Translational Medicine.** In press.

4. Basic insights into neurodegeneration. These studies used a cell-specific and region-specific transcriptomics approach to identify novel mechanisms underlying regional neuropathology in MS models and MS autopsy tissues. While this approach had been used in astrocytes during health, *my lab was the first to use a cell-specific and region-specific transcriptomics approach in any neurodegenerative disease model* (in 2018).
a. Itoh,Y. Voskuhl, R.R. (2017) Cell specificity dictates similarities in gene expression in multiple sclerosis, Parkinson's disease, and Alzheimer's disease. **PLoS One**, 12:e0181349, PMCID 5513529.
b. Itoh, N., Itoh, Tassoni, A., Ren, E., Kaito, M., Ohno, A., Y., Ao, Y., Farkhondeh, V., Johnsonbaugh, H., Burda, J. Sofroniew, M.V., Voskuhl, R.R. (2018) Cell-Specific and Region-Specific Transcriptomics in the multiple sclerosis model: Focus on astrocytes. **Proceedings of the National Academy of Sciences (PNAS)**, 115:E302-E309, PMCID: PMC5777065.
c. Voskuhl, R.R., Itoh, N., Tassoni, A., Matsukawa, M., Ren, E., Tse, V., Jang, E., Suen, T., Itoh, Y. (2019) Gene expression in oligodendrocytes during remyelination reveals cholesterol homeostasis as a therapeutic target in multiple sclerosis. **Proceedings of the National Academy of Sciences (PNAS)**, 116 (20):1-130-10139, PMCID: PMC6525478.
d. Tassoni, A., Farkhondeh, V., Itoh, Y., Itoh, N., Sofroniew, M.V., Voskuhl, R.R. (2019) The astrocyte transcriptome in EAE optic neuritis shows complement activation and reveals a sex difference in astrocytic C3 expression. **Scientific Reports**, 9:10010-22, PMCID: PMC6620300.
e. Voskuhl, R., MacKenzie-Graham, A., (2022) Chronic Experimental Autoimmune Encephalomyelitis is an Excellent Model to Study Neuroaxonal Degeneration in Multiple Sclerosis", **Frontiers in Molecular Neuroscience***. Vol. 15:* 10.3389/fnmol.2022.1024058.
f. Itoh, N., Itoh, Y., Stiles, L., Voskuhl, R.R. (2023) Sex differences in the neuronal transcriptome and synaptic mitochondrial function in cerebral cortex of a multiple sclerosis model. ***Frontiers in Neurology*** *Vol. 14*: doi: 10.3389/fneur.2023.1268411

5. Other Clinical Research. I initially studied immune responses in the peripheral blood of MS patients during the hormone treatment trials where I was the PI. Then I focused on the CNS. In collaboration with Dr. MacKenzie-Graham, *we mapped 3 different MS disabilities to distinct gray matter regions, which* was highlighted by an editorial in *JAMA Neurology. We also showed sex differences in regional gray matter atrophy in MS patients* by comparing gray matter atrophy in female MS vs female healthy controls and by comparing male MS vs male healthy controls (to remove the confound of sex differences in healthy brain).
a. Soldan, S.S., Alvarez-Retuerto, A.I., Sicotte, N.L., Voskuhl, R.R. (2003) Th1 to Th2 immune shift in female MS patients treated with the pregnancy hormone estriol, **Journal of Immunology,** 11:6267-6274.
b. Gold, S., Chalifoux, S., Giesser, B., Voskuhl, R.R. (2008) "Immune Modulation and Increased Neurotrophic Factor Production in Multiple Sclerosis Patients treated with Testosterone." **Journal of Neuroinflammation,** 5:32: 1-8. PMID: PMC2518142.
c. MacKenzie-Graham, A., Kurth, F., Itoh, Y., Wang, H., Montag, M., Elashoff, R., Voskuhl, R. (2016) Disability-Specific Atlases of Gray Matter Loss in Relapsing-Remitting Multiple Sclerosis. **JAMA Neurology**, 73:944-953, PMCID: 27294295
*(Editorial highlight in same issue of **JAMA Neurology, (**2016), 73(8):910-912.
d. Voskuhl, R.R., Patel, K., Paul, F., Gold, S.M., Scheel, M., Kuchling, J., Cooper, G., Asseyer, S., Chien, C., Brandt, A.U., Meyer, C.E., MacKenzie-Graham, A. (2020) Sex Differences in Brain Atrophy in Multiple Sclerosis. **Biology of Sex Differences**, 11(1):49. PMCID: PMC7456053.

Completed recent funding with R. Voskuhl as PI:

National Institutes of Health / NINDS / RO1	9/30/18 – 5/31/23	Total $2,194,376
#RO1NS109670	(PI Voskuhl)	

Title: Neuroprotection in MS: A Cell-specific and Region-specific Transcriptomics Approach
Goal: Understand neurodegenerative mechanisms in preclinical models of MS in females and males.

National Institutes of Health / NINDS / RO1	12/01/16 - 6/30/21	Total $2,138,929
#RO1NS096748	(PI Voskuhl)	

Parental imprinting of the X chromosome: Effects on neurodegeneration
Goal: Determine effects of X imprinting on gene expression in neuroimmunology